

WHAT IS CLAIMED IS:

1. An isolated nucleic acid encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:93-155.
2. An isolated nucleic acid encoding a polypeptide comprising an amino acid sequence selected from the group consisting of:
 - a) SEQ ID NO:111;
 - b) SEQ ID NO:120;
 - c) SEQ ID NO:121; and
 - d) SEQ ID NO:153.
3. An isolated nucleic acid encoding at least 7 contiguous amino acids of the amino acid sequence according to claim 1.
4. An isolated nucleic acid encoding at least 7 contiguous amino acids of the amino acid sequence according to claim 2.
5. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:
 - a) SEQ ID NO:1-92;
 - b) SEQ ID NO:156-693;
 - c) SEQ ID NO:694-979;
 - d) SEQ ID NO:980 to SEQ ID NO:1766; and
 - e) SEQ ID NO:1767 to SEQ ID NO:4687.
6. 6. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:
 - a) SEQ ID NO:19;
 - b) SEQ ID NO:31;

c) SEQ ID NO:32; and

d) SEQ ID NO:90.

..

7. An isolated nucleic acid comprising a nucleotide sequence which is 90% identical to the nucleotide sequence according to claim 5.
8. An isolated nucleic acid comprising a nucleotide sequence which is 90% identical to the nucleotide sequence according to claim 6.
9. An isolated nucleic acid comprising at least 15 contiguous nucleotides of the nucleotide sequence according to claim 5.
10. An isolated nucleic acid comprising at least 15 contiguous nucleotides of the nucleotide sequence according to claim 6.
11. An isolated nucleic acid comprising a nucleotide sequence which is complementary to the nucleotide sequence of the nucleic acid according to claim 9.
12. An isolated nucleic acid comprising a nucleotide sequence which is complementary to the nucleotide sequence of the nucleic acid according to claim 10.
13. A vector comprising the nucleic acid according to claim 3.
14. A vector comprising the nucleic acid according to claim 4.
15. A vector comprising the nucleic acid according to claim 9.
16. A vector comprising the nucleic acid according to claim 10.
17. A host cell comprising the vector according to claim 13, wherein the host cell is selected from the group consisting of bacterial, yeast, insect, mammalian, and plant cells.
18. A host cell comprising the vector according to claim 14, wherein the host cell is selected from the group consisting of bacterial, yeast, insect, mammalian, and plant cells.

19. A host cell comprising the vector according to claim 15, wherein the host cell is selected from the group consisting of bacterial, yeast, insect, mammalian, and plant cells.
20. A host cell comprising the vector according to claim 16, wherein the host cell is selected from the group consisting of bacterial, yeast, insect, mammalian, and plant cells.
21. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:93-155.
22. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:
- a) SEQ ID NO:111;
 - b) SEQ ID NO:120;
 - c) SEQ ID NO:121; and
 - d) SEQ ID NO:153.
23. An isolated polypeptide comprising an amino acid sequence which is 90% identical to the amino acid sequence according to claim 21.
24. An isolated polypeptide comprising an amino acid sequence which is 90% identical to the amino acid sequence according to claim 22.
25. An isolated polypeptide comprising at least 7 contiguous amino acids of the amino acid sequence according to claim 21.
26. An isolated polypeptide comprising at least 7 contiguous amino acids of the amino acid sequence according to claim 22.
27. An antibody or antibody fragment that binds to the polypeptide according to claim 25.
28. An antibody or antibody fragment that binds to the polypeptide according to claim 26.

29. The antibody or antibody fragment according to claim 27 which is monoclonal.
30. The antibody or antibody fragment according to claim 28 which is monoclonal.
31. A pharmaceutical composition comprising the nucleic acid according to claim 11, and a physiologically acceptable carrier, excipient, or diluent.
32. A pharmaceutical composition comprising the nucleic acid according to claim 12, and a physiologically acceptable carrier, excipient, or diluent.
33. A pharmaceutical composition comprising the vector according to claim 13, and a physiologically acceptable carrier, excipient, or diluent.
34. A pharmaceutical composition comprising the vector according to claim 14, and a physiologically acceptable carrier, excipient, or diluent.
35. A pharmaceutical composition comprising the vector according to claim 15, and a physiologically acceptable carrier, excipient, or diluent.
36. A pharmaceutical composition comprising the vector according to claim 16, and a physiologically acceptable carrier, excipient, or diluent.
37. A pharmaceutical composition comprising the polypeptide according to 25, and a physiologically acceptable carrier, excipient, or diluent.
38. A pharmaceutical composition comprising the polypeptide according to 26, and a physiologically acceptable carrier, excipient, or diluent.
39. A pharmaceutical composition comprising the antibody according to claim 29, and a physiologically acceptable carrier, excipient, or diluent.
40. A pharmaceutical composition comprising the antibody according to claim 30, and a physiologically acceptable carrier, excipient, or diluent.
41. An isolated nucleic acid variant comprising a nucleotide sequence selected from the group consisting of:

246

- a) SEQ ID NO:1 to SEQ ID NO:5;
- b) SEQ ID NO:17 to SEQ ID NO:18;
- c) SEQ ID NO:19;
- d) SEQ ID NO:20;
- e) SEQ ID NO:31 to SEQ ID NO:32;
- f) SEQ ID NO:36 to SEQ ID NO:37;
- g) SEQ ID NO:43 to SEQ ID NO:44;
- h) SEQ ID NO:74;
- i) SEQ ID NO:76;
- j) SEQ ID NO:80 to SEQ ID NO:81;

k) SEQ ID NO:90; which contains at least one single nucleotide polymorphism set forth in Table 10.

42. An isolated nucleic acid variant comprising at least 15 contiguous nucleotides of a nucleotide sequence selected from the group consisting of:

- a) SEQ ID NO:1 to SEQ ID NO:5;
- b) SEQ ID NO:17 to SEQ ID NO:18;
- c) SEQ ID NO:19;
- d) SEQ ID NO:20;
- e) SEQ ID NO:31 to SEQ ID NO:32;
- f) SEQ ID NO:36 to SEQ ID NO:37;
- g) SEQ ID NO:43 to SEQ ID NO:44;
- h) SEQ ID NO:74;
- i) SEQ ID NO:76;

j) SEQ ID NO:80 to SEQ ID NO:81;

k) SEQ ID NO:90; which contains at least one single nucleotide polymorphism set forth in Table 10.

43. An isolated nucleic acid variant comprising at least 15 contiguous nucleotides of a nucleotide sequence set forth in SEQ ID NO:16, which contains at least one single nucleotide polymorphism selected from the group consisting of SNP E 2, SNP H 1, SNP F -2, SNP O 1, SNP O 6, SNP M 1, and SNP M +1.

44. An isolated nucleic acid variant comprising at least 15 contiguous nucleotides of a nucleotide sequence set forth in SEQ ID NO:90, which contains at least one single nucleotide polymorphism selected from the group consisting of SNP A 2, SNP A +4, and SNP A 4.

45. An isolated nucleic acid variant comprising at least 15 contiguous nucleotides of a nucleotide sequence set forth in SEQ ID NO:31 or SEQ ID NO:32, which contains at least one single nucleotide polymorphism selected from the group consisting of SNP Y +1 and SNP H 1.

46. An isolated nucleic acid comprising a nucleotide sequence that is complementary to the nucleotide sequence of the nucleic acid according to claim 42.

47. An isolated alternate splice variant comprising a nucleotide sequence selected from the group consisting of:

- a) SEQ ID NO:1 to SEQ ID NO:5;
- b) SEQ ID NO:17 to SEQ ID NO:18;
- c) SEQ ID NO:31 to SEQ ID NO:32;
- d) SEQ ID NO:36 to SEQ ID NO:37;
- e) SEQ ID NO:43 to SEQ ID NO:44; and
- f) SEQ ID NO:80 to SEQ ID NO:81.

48. An isolated alternate splice variant comprising at least 15 contiguous nucleotides of a nucleotide sequence selected from the group consisting of:

- a) SEQ ID NO:1 to SEQ ID NO:5;
- b) SEQ ID NO:17 to SEQ ID NO:18;
- c) SEQ ID NO:31 to SEQ ID NO:32;
- d) SEQ ID NO:36 to SEQ ID NO:37;
- e) SEQ ID NO:43 to SEQ ID NO:44; and
- f) SEQ ID NO:80 to SEQ ID NO:81.

49. An isolated nucleic acid comprising a nucleotide sequence that is complementary to the nucleotide sequence according to claim 48.

50. An isolated polypeptide encoded by the nucleic acid variant according to claim 41.

51. An isolated polypeptide encoded by the alternate splice variant according to claim 47.

52. An antibody or antibody fragment that binds to the polypeptide according to claim 50.

53. An antibody or antibody fragment that binds to the polypeptide according to claim 51.

54. The antibody or antibody fragment according to claim 52 which is monoclonal.

55. The antibody or antibody fragment according to claim 53 which is monoclonal.

56. A kit for detecting a 12q23-qter nucleotide sequence comprising:

- a) the isolated nucleic acid according to claim 9; and

b) at least one component to detect hybridization of the isolated nucleic acid to a 12q23-qter nucleotide sequence.

57. A kit for detecting a 12q23-qter nucleotide sequence comprising:

a) the isolated nucleic acid according to claim 11; and

b) at least one component to detect hybridization of the isolated nucleic acid to a 12q23-qter nucleotide sequence.

58. A kit for detecting a 12q23-qter nucleotide sequence comprising:

a) the isolated nucleic acid according to claim 42; and

b) at least one component to detect hybridization of the isolated nucleic acid to a 12q23-qter nucleotide sequence.

59. A kit for detecting a 12q23-qter nucleotide sequence comprising:

a) the isolated nucleic acid according to claim 46; and

b) at least one component to detect hybridization of the isolated nucleic acid to a 12q23-qter nucleotide sequence.

60. A kit for detecting a 12q23-qter amino acid sequence comprising:

a) the antibody or antibody fragment according to claim 29; and

b) at least one component to detect binding of the antibody to a 12q23-qter amino acid sequence.

61. A kit for detecting a 12q23-qter amino acid sequence comprising:

a) the antibody or antibody fragment according to claim 54; and

b) at least one component to detect binding of the antibody to a 12q23-qter amino acid sequence.

62. A method of diagnosing a 12q23-qter-associated disorder in a human subject, comprising:

a) contacting the nucleic acid according to claim 42 with a biological sample obtained from the subject;

b) incubating the nucleic acid and biological sample under high stringency conditions that allow the nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; and

c) detecting the hybridization complex of (b), wherein detection of the complex indicates diagnosis of a 12q23-qter-associated disorder.

63. The method of claim 62, wherein the disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

64. A method of diagnosing a 12q23-qter-associated disorder in a human subject, comprising:

a) contacting the antibody or antibody fragment according to claim 54 with a biological sample obtained from the subject;

b) incubating the antibody or antibody fragment and biological sample under conditions to allow the antibody or antibody fragment to bind to an amino acid sequence in the sample, and thereby form a complex; and

c) detecting the complex of (b), wherein detection of the complex indicates diagnosis of a 12q23-qter-associated disorder.

65. The method according to claim 64, wherein the disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

66. A method of determining a 12q23-qter pharmacogenetic profile for a human subject comprising:

a) contacting the nucleic acid according to claim 42 with a biological sample obtained from the subject;

b) incubating the nucleic acid and biological sample under high stringency conditions to allow the nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; ...

c) detecting the hybridization complex of (b), wherein detection of the complex determines the 12q23-qter pharmacogenetic profile.

67. A method of determining a 12q23-qter pharmacogenetic profile for a human subject comprising:

a) contacting the antibody or antibody fragment according to claim 54 with a biological sample obtained from the subject;

b) incubating the antibody or antibody fragment with the biological sample under conditions that allow the antibody to bind to an amino acid sequence in the sample, and thereby form a complex; and

c) detecting the complex of (b), wherein detection of the complex determines the 12q23-qter pharmacogenetic profile.

68. A method of identifying an ortholog of a human 12q23-qter gene, comprising:

a) contacting the isolated nucleic acid according to claim 3 with a biological sample obtained from a non-human animal;

b) incubating the nucleic under conditions that allow the nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; and

c) detecting the hybridization complex of (a), wherein detection of the complex indicates identification of an ortholog of a human 12q23-qter gene.

69. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the vector according to claim 13, and a physiologically acceptable carrier, excipient, or diluent, in an amount effective to treat the disorder.

70. The method according to claim 69, wherein the 12q23-qter-associated disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

71. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the host cell according to claim 17, and a physiologically acceptable carrier, excipient, or diluent, in an amount effective to treat the disorder.

72. The method according to claim 71, wherein the 12q23-qter-associated disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

73. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the isolated nucleic acid according to claim 46, and a physiologically acceptable carrier, excipient or diluent, in an amount effective to treat the disorder.

74. The method according to claim 73, wherein the 12q23-qter-associated disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

75. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the isolated polypeptide according to claim 25, and a physiologically acceptable carrier, excipient or diluent, in an amount effective to treat the disorder.

76. The method according to claim 75, wherein the 12q23-qter-associated disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

77. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the antibody or antibody fragment according to claim 54, and a physiologically acceptable carrier, excipient or diluent, in an amount effective to treat the disorder.

78. The method according to claim 77, wherein the 12q23-qter-associated disorder is selected from the group consisting of asthma, obesity, and inflammatory bowel disease.

79. A transgenic mouse whose genome comprises an introduced null mutation in an endogenous gene which is orthologous to a human 12q23-qter gene comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:92.

80. The transgenic mouse according to claim 79, wherein both alleles of the endogenous gene have been disrupted.

81. The transgenic mouse according to claim 80, wherein the mouse genome further comprises a human 12q23-qter nucleotide sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:92 and SEQ ID NO:156 to SEQ ID NO:4687.

82. A method of making a homozygous transgenic knockout mouse comprising:

a) disrupting an endogenous gene in mouse embryonic stem cells, wherein the endogenous gene is orthologous to a human 12q23-qter gene comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:92;

- b) introducing said embryonic stem cells into a mouse blastocyst and transplanting said blastocyst into a pseudopregnant mouse;
- c) allowing said blastocyst to develop into a chimeric mouse;
- d) breeding said chimeric mouse to produce offspring; and
- e) screening said offspring to identify a homozygous transgenic knockout mouse.

83. A method of forming a crystal of the isolated polypeptide according to claim 25 comprising:

- a) incubating the polypeptide with a solution selected from the group consisting of the solutions in wells 1-30 in Table 1A under conditions to allow crystalization; and
- b) detecting the crystalization in (a), whereby crystalization indicates formation of a crystal.

84. A cell line comprising the isolated nucleic acid according to claim 3.

85. A biochip comprising the isolated nucleic acid according to claim 9.

86. An isolated nucleic acid variant encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:93-155, which contains at least one amino acid change set forth in Table 10.

87. An isolated nucleic acid variant encoding a polypeptide comprising an amino acid sequence selected from the group consisting of:

- a) SEQ ID NO:111;
- b) SEQ ID NO:120;
- c) SEQ ID NO:121; and
- d) SEQ ID NO:153; which contains at least one amino acid change set forth in Table 10.

88. An isolated nucleic acid probe comprising at least 8 contiguous nucleotides of a nucleotide sequence selected from Table 8.

89. An isolated nucleic acid probe comprising at least 8 contiguous nucleotides of a nucleotide sequence selected from Table 9.

90. An isolated nucleic acid probe comprising at least 8 contiguous nucleotides of a nucleotide sequence selected from Table 11A.

91. An isolated nucleic acid probe comprising at least 8 contiguous nucleotides of a nucleotide sequence selected from Table 11B.

92. A method of diagnosing a 12q23-qter-associated disorder in a human subject, comprising:

a) contacting the isolated nucleic acid according to claim 88 with a biological sample obtained from the subject;

b) incubating the isolated nucleic acid and biological sample under high stringency conditions that allow the isolated nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; and

c) detecting the hybridization complex of (b), wherein detection of the complex indicates a diagnosis of a 12q23-qter-associated disorder.

93. A method of diagnosing a 12q23-qter-associated disorder in a human subject, comprising:

a) contacting the isolated nucleic acid according to claim 89 with a biological sample obtained from the subject;

b) incubating the isolated nucleic acid and the biological sample under high stringency conditions that allow the isolated nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; and

c) detecting the hybridization complex of (b), wherein detection of the complex indicates diagnosis of a 12q23-qter-associated disorder.

94. A method of diagnosing a 12q23-qter-associated disorder in a human subject, comprising:

- a) contacting the isolated nucleic acid according to claim 90 with a biological sample obtained from the subject;
- b) incubating the isolated nucleic acid and the biological sample under high stringency conditions that allow the isolated nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; and
- c) detecting the hybridization complex of (b), wherein detection of the complex indicates diagnosis of a 12q23-qter-associated disorder.

95. A method of diagnosing a 12q23-qter-associated disorder in a human subject, comprising:

- a) contacting the isolated nucleic acid according to claim 91 with a biological sample obtained from the subject;
- b) incubating the isolated nucleic acid and the biological sample under high stringency conditions that allow the isolated nucleic acid to hybridize to a nucleic acid in the sample, and thereby form a complex; and
- c) detecting the hybridization complex of (b), wherein detection of the complex indicates diagnosis of a 12q23-qter-associated disorder.

96. An isolated antisense nucleic acid comprising the nucleotide sequence according to claim 11.

97. An isolated antisense nucleic acid comprising the nucleotide sequence according to claim 12.

98. An isolated antisense nucleic acid comprising the nucleotide sequence according to claim 46.

99. An isolated antisense nucleic acid comprising the nucleotide sequence according to claim 49.

100. A method of identifying a 12q23-qter ligand, comprising:

a) contacting the isolated polypeptide according to claim 25 with a test agent;

b) incubating the isolated polypeptide and the test agent under conditions that allow the polypeptide to bind to the test agent, and thereby form a complex; and

c) detecting the complex of (b), wherein detection of the complex indicates identification of a 12q23-qter ligand.

101. A method of identifying a 12q23-qter ligand, comprising:

a) contacting a polypeptide comprising at least 7 contiguous amino acids of the isolated polypeptide according to claim 50 with a test agent;

b) incubating the polypeptide and the test agent under conditions that allow the polypeptide to bind to the test agent, and thereby form a complex; and

c) detecting the complex of (b), wherein detection of the complex indicates identification of a 12q23-qter ligand.

102. A method of identifying a 12q23-qter ligand, comprising:

a) contacting the isolated nucleic acid according to claim 9 with a test agent;

b) incubating the isolated nucleic acid and the test agent under conditions that allow the nucleic acid to bind to the test agent, and thereby form a complex; and

c) detecting the complex of (b), wherein detection of the complex indicates identification of a 12q23-qter ligand.

103. A method of identifying a 12q23-qter ligand, comprising:

a) contacting the isolated nucleic acid according to claim 42 with a test agent;

b) incubating the isolated nucleic acid and the test agent under conditions that allow the nucleic acid to bind to the test agent, and thereby form a complex; and ..

c) detecting the complex of (b), wherein detection of the complex indicates identification of a 12q23-qter ligand.

104. The method according to claim 100, wherein the test agent comprises a small molecule.

105. The method according to claim 101, wherein the test agent comprises a small molecule.

106. The method according to claim 102, wherein the test agent comprises a small molecule.

107. The method according to claim 103, wherein the test agent comprises a small molecule.

108. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the ligand isolated by the method according to claim 100, and a physiologically acceptable carrier, excipient or diluent, in an amount effective to treat the disorder.

109. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the ligand isolated by the method according to claim 101, and a physiologically acceptable carrier, excipient or diluent, in an amount effective to treat the disorder.

110. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the ligand isolated by the method according to claim 102, and a physiologically acceptable carrier, excipient or diluent, in an amount effective to treat the disorder.

111. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the ligand isolated by the method according to claim 103, and a physiologically acceptable carrier, excipient or diluent, in an amount effective to treat the disorder.

111. A method of treating a 12q23-qter-associated disorder in a human subject comprising administering to the subject a pharmaceutical composition which comprises the ligand isolated by the method according to claim 103, and a physiologically acceptable carrier, excipient or diluent, in an amount effective to treat the disorder.